Claim 16 is amended. As a result, claims 2-8, and 10-25 are now pending in this application. No new subject matter has been added. The amendments are made to clarify the claims, and not for reasons relating to patentability. Therefore, the amendments are not intended to limit the scope of equivalents to which any claim element may be entitled.

§112 Rejection of the Claims

The Advisory Action dated October 2, 2001 indicated that the transition phrase "consisting essentially of" has not been adequately defined.

The present invention is directed to a new cloning system for generating recombinant adenovirus that uses two components (a) an Ad backbone plasmid consisting essentially of an Ad genome lacking map units 0 to 9.2, and (b) a shuttle plasmid consisting essentially of Ad sequences from 0 to 1 and 9.2 to 16.1 map units of an Ad genome. This new cloning system overcomes shortcomings of previously-known systems, such as the time required to generate the vectors and wildtype contamination in the initial plaque isolation that necessitates further, time intensive serial plaque isolations and amplification. Specification at page 2, line 16 to page 3, line 17. A system that uses *in vitro* enzymatic recombination using Cre-loxP shuttles and backbone viral DNA was specifically discussed in the specification as also having drawbacks. The present inventors set out to create a new cloning system that did not require the use of Cre-loxP shuttles, and would thus overcome its problems.

The transition phrase "consisting essentially of" in common patent law parlance has been defined to cover combinations with some additional elements, but excludes additional unspecified ingredients which would affect the basic and novel characteristics of the product defined in the balance of the claim." *Atlas Powder C. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1574, 224 USPQ 409, 412 (Fed. Cir. 1984) (phrase "consisting essentially of" "excludes ingredients that would 'materially affect the basic and novel characteristics' of the claimed composition."); *In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221 (CCPA 1960) ("the 'consisting essentially of' terminology would . . . exclude additional unspecified ingredients which would affect the basic an novel characteristics of the product defined int h balance of the

claim."); *In re Janakirama-Rao*, 317 F.2d 951, 954, 137 USPQ 893 (CCPA 1963) ("The word 'essentially' opens the claims to the inclusion of ingredients which do *not* materially affect the basic and novel characteristics of appellant's compositions as defied in th balance of the claims."). The Federal Circuit in *PPG Industries v. Guardian Industries Corp.*, 156 F.3d 1351, 1354, 48 USPQ2d 1351, 1353-1354 (1998) stated the following:

> "'Consisting essentially of' is a transition phrase commonly used to signal a partially open claim in a patent. Typically, 'consisting essentially of' precedes a list of ingredients in a composition claim or a series of steps in a process claim. By using the term 'consisting essentially of,' the drafter signals that the invention necessarily includes the listed ingredients and is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention. A 'consisting essentially of' claim occupies a middle ground between closed claims that are written in a 'consisting of' format and fully open claims that are drafted in a 'comprising' format."

The present invention is directed to a cloning system that includes an Ad backbone plasmid consisting essentially of an Ad genome lacking map units 0 to 9.2 and a shuttle plasmid consisting essentially of Ad sequences from 0 to 1 and 9.2 to 16.1 map units of an Ad genome. The present cloning system specifically excludes the well-known cre-lox recombination system, as the inclusion of cre-lox sequences would materially affect the basic and novel characteristics of the present invention. The claims as currently amended meet the adequate description requirement of 35 U.S.C. §112, first paragraph.

§102 Rejection of the Claims

Claims 4-6, 10, 11, 13-19 and 22-26 were rejected under 35 U.S.C. § 102(a) as being anticipated by Aoki et al. A proper rejection under §102(b) requires that a cited reference identically describe or disclose all of the elements of the claimed invention. Aoki *et al.* discuss an adenoviral vector that uses the cre-loxP system. Aoki *et al.*, however, do not teach a cloning system that includes an Ad backbone plasmid consisting essentially of an Ad genome lacking map units 0 to 9.2 and a shuttle plasmid consisting essentially of Ad sequences from 0 to 1 and

9.2 to 16.1 map units of an Ad genome. Aoki *et al.*, therefore, does not identically describe or disclose all of the elements of the claimed invention.

Applicant respectfully requests that the rejections under 35 U.S.C. § 102(b) be withdrawn.

§103 Rejection of the Claims

A. Claims 2, 3, 20 and 21

Claims 2, 3, 20 and 21 were rejected under 35 USC § 103(a) as being unpatentable over Aoki *et al.* in view of Krougliack *et al.*

As discussed above, the claims of the present invention recite a cloning system that uses adenoviral backbone vectors that lack a loxP sequence, whereas Aoki *et al.* discuss an adenovirus backbone (cosmid) vector that uses the Cre-loxP system. Therefore, Aoki *et al.* does not teach or suggest all of the claim limitations as required for obviousness.

Krougliak *et al.* does not remedy the deficiencies of Aoki *et al.* There is no suggestion or motivation, either in the cited references themselves or in the knowledge generally available to an art worker, to modify the references or to combine the teachings of the references so as to arrive at the claimed invention. Pending claims 2, 3, 20 and 21 recite a two-part cloning system; the first element being a backbone plasmid consisting essentially of map units 9.2 to 100 of an Ad genome, and the second element being a shuttle plasmid consisting essentially of 0 to 1 and 9.2 to 16.1 map units of an Ad genome. Krougliak *et al.* generated cell lines that could complement E1, E4 and protein IX defective adenovirus type 5 (Ad5) mutants. The plasmid system used by Krougliak *et al.* contained adenovirus sequences from the left ITR to the right ITR (*i.e.*, the full viral backbone), except for sequences encoding E1, E4 or protein IX. The intention of the deletions by Krougliak *et al.* was to provide for more space to accommodate larger inserts placed into the E1 region of the adenovirus vector and not to otherwise modify the backbone. If one of skill in the art logically combined these two references one would develop a full-length adenoviral vector (except that it lacks sequences encoding E1, E4 or protein IX) that uses the Cre-loxP system in a cell line that complements E1, E4 and protein IX defective Ad5

mutants. The present invention is distinguishable over such a system in that the cloning system of the present invention specifically lacks the lefthand ITR and loxP sequences in the backbone and shuttle plasmids.

Thus, neither of these references, either alone or taken in combination, teach the present claimed invention. Therefore, Applicant respectfully requests that this rejection under 35 U.S.C. § 103 be withdrawn.

B. Claims 7-8

Claims 7-9 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Aoki *et al.* and Krougliak *et al.* and further in view of Breakfield *et al.* (U.S. 5,965,441).

Claims 7-8 (claim 9 having been cancelled) have been amended to recite a two-plasmid cloning system where both the shuttle and backbone plasmids lack loxP sequences. As discussed above, this cloning system is distinguishable over Aoki *et al.* in view of Krougliak *et al.* because the backbone used in the present system lacks the lefthand ITR and loxP sequences.

Breakfield *et al.* does not remedy the shortcomings of Aoki *et al.* combined with Krougliak *et al.* Breakfield *et al.* teach a hybrid vector system that incorporate elements of herpesvirus and adeno-associated virus that is capable of expressing a gene product in eukaryotic cells. The Examiner admits that Breakfield *et al.* is deficient in that it does not teach an adenovirus vector. The Examiner states, however, that "one of ordinary skill in the art at the time was made would have been motivated to apply the AAV/HSV hybrid vector taught by Breakfield *et al.* to the fast method for generating recombinant Ad viruses without contamination of the wild type virus taught by Aoki *et al.* with the cell line that successfully produced recombinant adenoviruses that have large sections deleted from them taught by Krougliak *et al.*" Applicant respectfully reminds the Examiner, however, that the "fast method for generating recombinant Ad viruses" taught by Aoki *et al.* requires the use of Cre-loxP, which is different from the present invention. Therefore, if these three references are logically combined, one would have the Aoki *et al.* Ad vector containing a loxP sequence and the Breakfield *et al.* AAV/HSV hybrid sequences in the Krougliak *et al.* cell line (in a backbone containing the

lefthand ITR). In contrast, the plasmids used in the present claimed cloning system do not contain loxP sequences or the lefthand ITR.

Therefore, Applicant respectfully requests that this rejection under 35 U.S.C. § 103 be withdrawn.

C. Claim 12

Claim 12 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Aoki *et al.*, Krougliak *et al.*, and Breakfield *et al.* as applied to claims 1-11 and 13-25 above, and further in view of Chartier *et al.* Aoki *et al.*, Krougliak *et al.*, and Breakfield *et al.* are discussed above. Chartier *et al.* do not remedy the deficiencies of Aoki *et al.*, Krougliak *et al.*, and Breakfield *et al.* Chartier *et al.* disclose the introduction of unique PacI site into and Ad5 vector.

There is no suggestion or motivation in the cited references to combine the teachings of the references so as to arrive at the claimed invention. Claim 12 recites a shuttle plasmid having Ad sequences wherein PacI restriction endonuclease sites flank either end of the Ad sequences, but wherein the plasmid lacks a loxP sequence. If Aoki *et al.*, Krougliak *et al.*, Breakfield *et al.* and Chartier *et al.* are combined, one would have the Aoki *et al.* Ad vector containing a loxP sequence, the Breakfield *et al.* AAV/HSV hybrid sequences and the Chartier *et al.* PacI sites in the Krougliak *et al.* cell line (in a backbone containing the lefthand ITR). In contrast, the present claimed invention does not contain loxP sequences or the lefthand ITR.

Therefore, Applicant respectfully requests that this rejection under 35 U.S.C. § 103 be withdrawn.

Conclusion

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (612-373-6961) to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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